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(FILE 'HOME' ENTERED AT 11:13:44 ON 19 JUN 2003)
     FILE 'CAPLUS' ENTERED AT 11:17:24 ON 19 JUN 2003
              27 S PAROXETINE AND AMMONI?
L1
L2
              21 S L1 AND AMMONIUM
=> s 12 and quarte?
          17269 QUARTE?
              0 L2 AND QUARTE?
L3
=> d bib abs 12 1-21
L2
     ANSWER 1 OF 21 CAPLUS COPYRIGHT 2003 ACS
ΑN
     2003:202635 CAPLUS
DN
     138:243277
ΤI
     Paroxetine isethionate salt, process of preparation and use in
     the treatment of depression
     Callewaert, George Leo
IN
PA
     Spurcourt Limited, UK
SO
     PCT Int. Appl., 42 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
FAN.CNT 1
     PATENT NO.
                        KIND
                               DATE
                                                APPLICATION NO.
                               _____
                                                -----
PΤ
     WO 2003020717
                        A1
                               20030313
                                               WO 2002-GB3377
                                                                   20020724
              AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
              TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
              CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
              NE, SN, TD, TG
PRAI GB 2001-18869
                               20010802
                         Α
     GB 2001-27203
                         Α
                               20011109
AΒ
     A salt in cryst. form derived from isethionic acid and paroxetine
     free base is described. The paroxetine isethionate salt
     together with a pharmaceutically acceptable carrier, diluent or excipient
     is formulated into dosage forms, e.g., tablets, useful for the treatment
     of a disease state ameliorated by administration of a 5-HT uptake
     inhibitor, e.g., depression or anxiety.
               THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 2 OF 21 CAPLUS COPYRIGHT 2003 ACS
L_2
     2003:133042 CAPLUS
ΑN
DN
     138:175879
TI
     Preparation of paroxetine glycyrrhizinate pharmaceuticals
IN
     Barges Causeret, Nathalie Claude Marianne; Marzolini, Nicola Lisa Anna;
     Meneaud, Padma
PA
     Smithkline Beecham PLC, UK
SO
     PCT/Int. Appl., 14 pp.
     CODEN: PIXXD2
דת
     Patent
LA
     English
FAN.CNT 2
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APPLICATION NO. DATE
                      KIND DATE
     PATENT NO.
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                             20030220
                                           WO 2002-EP8926 20020809
     WO 2003013529
                       A1
PΙ
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRAI GB 2001-19467
                      Α
                             20010809
     The title salt (I) formed from paroxetine-HCl hydrochloride and
     ammonium glycyrrhizinate masks the bitter taste of
     paroxetine and has a distinctive licorice flavor. Tablets were
     obtained from I 20.00, dicalcium phosphate 83.34, microcryst. cellulose
     50.67, sodium starch glycolate 8.34, and Mg stearate 1.67 mg.
              THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 3 OF 21 CAPLUS COPYRIGHT 2003 ACS
L2
     2003:132991 CAPLUS
AN
DN
     138:175862
TI
     Composition comprising paroxetine and a glycyrrhizinate salt
     Barges Causeret, Nathalie Claude Marianne; Marzolini, Nicola Lisa Anna;
IN
     Meneaud, Padma
     Smithkline Beecham PLC, UK
PA
so
     PCT Int. Appl., 13 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 2
     PATENT NO.
                      KIND
                             DATE
                                             APPLICATION NO. DATE
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                             _____
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                                         WO 2002-EP8925 20020809
     WO 2003013470
                      A1
                             20030220
PΙ
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRAI GB 2001-19467
                       Α
                             20010809
     GB 2001-19468
                        Α
                             20010809
     GB 2001-19469
                             20010809
                        Α
                             20010809
     GB 2001-19470
                        Α
AΒ
     A taste-masked formulation of paroxetine comprises a dry blend
     of paroxetine and a glycyrrhizinate, esp. paroxetine
     hydrochloride and ammonium glycyrrhizinate, as a dispersible
     powder or molded into a dispersible or chewable tablet. Thus, a
     formulation contained paroxetine-HCl 22.80, ammonium
     glycyrrhizinate 14.00, Crospovidone 25.00, Pearlitol SD200 73.00,
     microcryst. cellulose 100.0, aspartame 12.00, and Mg stearate 2.50 mg.
              THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 6
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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2002:977660 CAPLUS
ΑN
DN
     138:29184
     A process for preparing paroxetine hydrochloride limiting
TI
     formation of pink compounds
IN
     Avrutov, Ilya; Pilarski, Gideon
PA
     Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,
     Inc.
SO
     PCT Int. Appl., 25 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                    KIND DATE
                                          APPLICATION NO. DATE
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                                          -----
                   A1
PΙ
     WO 2002102382
                           20021227
                                          WO 2002-US19016 20020614
     WO 2002102382
                     C2
                           20030306
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                           20030501
                                         US 2002-172521 20020614
     US 2003083501
                     A1
PRAI US 2001-298603P
                      Р
                           20010614
     US 2001-326993P
                      Ρ
                           20011005
     US 2002-346048P
                      P
                           20020104
AB
     The present invention provides a process for prepg. paroxetine
     -HCl (I) from paroxetine base which provides I substantially
     free of pink-colored compds. or an impurity identified by an HPLC RRT of
     about 1.5. The processes utilize a buffer, a molar ratio of HCl to
     paroxetine base of <1, and crystallize/recrystallize in the
     presence of an effective amt. of an anti-oxidant. A preferred way to
     create a buffer is by using ammonium chloride. A preferred
     anti-oxidant is ascorbic acid. The present invention also provides for
     re-crystg. I prepd. by the above methods or any other methods in the
     presence of an effective amt. of an anti-oxidant such as ascorbic acid. A
     preferred solvent system for recrystn. is a mixt. of acetone and methanol.
     Processes of the present invention can combine these various features. An
     aq. soln. of ammonium chloride in water was added to a soln. of
    paroxetine base in toluene. The reaction mixt. was intensively
     stirred at ambient temp. while concd. HCl was added in such manner that
     the pH of the reaction mixt. stayed between 3.5 and 8. A ppt. formed
     which was filtered and then washed with toluene and water. The resulting
     material was dried at 60.degree. under vacuum to give I. The soln. did
     not develop a pink color after standing for 20 min.
             THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
L2
    ANSWER 5 OF 21 CAPLUS COPYRIGHT 2003 ACS
     2002:964931 CAPLUS
AN
DN
     138:29172
ΤI
     Transdermal and topical administration of antidepressant drugs using basic
    Hsu, Tsung-Min; Hickey, Alan T. J.; Luo, Eric C.; Obara, Jane
IN
PA
SO
    U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 972,008.
     CODEN: USXXCO
\mathtt{DT}
    Patent
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ANSWER 4 OF 21 CAPLUS COPYRIGHT 2003 ACS

L2

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English
LА
FAN.CNT 22
                     KIND DATE
     PATENT NO.
                                         APPLICATION NO. DATE
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                    A1
    US 2002192302
                           20021219
                                          US 2002-175769
                                                          20020619
PI
                     A1
    US 2001051166
                           20011213
                                          US 2000-738410
                                                          20001214
    US 2002034554
US 1999-467
                     A1
                           20020214
                                          US 2000-738395
                                                          20001214
                     A1
                          20020321
                                          US 2001-972008
                                                          20011004
PRAI US 1999-465098 A2
                           19991216
                     A2
    US 2000-569889
                           20000511
    US 2000-607892
                    B2
                           20000630
    US 2000-738395
                    A2
                          20001214
    US 2000-738410
                     A2
                           20001214
    US 2001-972008
                      A2
                           20011004
    Methods are provided for enhancing the permeability of skin or mucosal
AΒ
    tissue to topical or transdermal application of antidepressant drugs.
    methods entail the use of a base in order to increase the flux of the drug
     through a body surface while minimizing the likelihood of skin damage,
     irritation or sensitization. The permeation enhancer can be an inorg. or
     org. base. Compns. and transdermal systems are also described.
L2
    ANSWER 6 OF 21 CAPLUS COPYRIGHT 2003 ACS
AN
    2002:946194 CAPLUS
DN
    138:25517
ΤI
    Production of molded articles by injection molding of compositions based
    on quaternary ammonium group-containing acrylic polymers
     Petereit, Hans-Ulrich; Beckert, Thomas; Assmus, Manfred; Hoess, Werner;
IN
    Fuchs, Wolfgang; Schikowsky, Hartmut
PA
    Roehm G.m.b.H. & Co. K.-G., Germany
    PCT Int. Appl., 40 pp.
SO
     CODEN: PIXXD2
DΤ
     Patent
LΑ
    German
FAN.CNT 1
                     KIND DATE
                                  APPLICATION NO. DATE
     PATENT NO.
                     ____
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                                         -----
                                    WO 2002-EP5041 20020508
PΙ
    WO 2002098625 A1 20021212
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
            HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
            LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
            UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                        DE 2001-10127134 20010605
    DE 10127134
                      A1
                           20021212
PRAI DE 2001-10127134 A
                           20010605
    Molded materials are produced by injection molding process comprising
     steps of (a) melting and mixing (meth)acrylate copolymers comprising
     85-98% of radically polymd. C1-C4-alkyl esters of acrylic or methacrylic
    acid and 2-15% of (meth)acrylate monomers having a quaternary
     ammonium group in the alkyl radical, 10-25% of a plasticizer,
    10-50% of an anti-adhesive agent, and/or 0.1-3% of a parting agent,
    optionally, other pharmaceutical additives or auxiliary agents and/or an
    active pharmaceutical ingredient, (b) degassing the mixt. at temps. of at
    least 120.degree. to the point where the content of the low-boiling
    constituents having vapor pressure of at least 1.9 bar at 120.degree. is
    reduced to .ltoreq. 0.5%, and (c) injecting the degassed mixt. at
    80-160.degree. into the mold of an injection molding unit and removing the
    molded body from the mold. The molded materials are intended for use as
    drug delivery systems and made in the form of plates where the active
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pharmaceutical ingredient is distributed in the compn. or in the form of

capsules where the active pharmaceutical ingredient is encapsulated. Thus, a compn. was prepd. by melt-extruding a mixt. of a trimethylammonium group-contg. acrylic copolymer (Eudragit RL 100), talc and tri-Et citrate plasticizer. Plates having even and smooth surface with const. refraction were produced by injection molding of this compn. at 120.degree..

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2003 ACS
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AN 2002:811964 CAPLUS

DN 137:299967

TI Unloaded ion exchange resins for the extended release of active ingredients

IN Hughes, Lyn; Bellamy, Simon Andrew; Hann, Christina

PA Rohm and Haas Company, USA

SO Eur. Pat. Appl., 13 pp. CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

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	PA	rent	NO.		KI	ND	DATE			A.	PPLI	CATI	ON NO	٥.	DATE			
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ΡI	EP 1250920			A1		20021023			EP 2002-252512			20020408						
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
			ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR						
	US	US 2002176842		A.	A1 20021128			US 2002-107288			20020326							
	JP	2003	0125	00	A:	2	2003	0115		J	P 20	02-1	0642	5	2002	0409		
PRAI	US	2001	-282	442P	P		2001	0409										

AB A dosage form is described that gives an extended release of ionizable active ingredients using unloaded ion exchange resins, that does not require the manuf. of a resinate. The release and absorption rate of the ionizable active ingredient from the dosage form can be modified by changing variables, i.e., degree of crosslinking, particle size, and the pK of the functional groups of unloaded ion exchange resin, the pK, mol. wt., and soly. in the release medium of the active ingredient, the ionic strength and pH of the release medium, temp., and coating the unloaded ion exchange resin with a permeable membrane. For example, a dosage form with sustained drug release was prepd. using 51.7 mg of diclofenac sodium and 75.9 mg of unloaded, unconditioned, anion exchange resin cholesterylamine that had been screened to remove particles of >37 .mu..

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2003 ACS
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AN 2002:754995 CAPLUS

DN 137:268473

TI Porous drug matrices and methods of manufacture thereof

IN Straub, Julie; Altreuter, David; Bernstein, Howard; Chickering, Donald E.;
Khattak, Sarwat; Randall, Greg

PA Acusphere Inc., USA

SO U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. 6,395,300. CODEN: USXXCO

DT Patent

LA English

FAN CNT 2

ENT NO.	KIND	DATE	APPLICATION NO.	DATE		
2002142050	A1	20021003	US 2002-53929	20020122		
6395300	B1	20020528	US 1999-433486	19991104		
1999-136323P	P	19990527				
1999-158659P	P	19991008				
1999-433486	A2	19991104				
	ENT NO. 2002142050 6395300 1999-136323P 1999-158659P	ENT NO. KIND	ENT NO. KIND DATE 2002142050 A1 20021003 6395300 B1 20020528 1999-136323P P 19990527 1999-158659P P 19991008	ENT NO. KIND DATE APPLICATION NO. 2002142050 A1 20021003 US 2002-53929 6395300 B1 20020528 US 1999-433486 1999-136323P P 19990527 1999-158659P P 19991008		

AB Drugs, esp. low aq. soly. drugs, are provided in a porous matrix form,

preferably microparticles, which enhances dissoln. of the drug in aq. media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aq. soly., in a volatile solvent to form a drug soln., (ii) combining at least one pore forming agent with the drug soln. to form an emulsion, suspension, or second soln. and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystn., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second soln. to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in cryst. form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystn. The pore forming agent can be either a volatile liq. that is immiscible with the drug solvent or a volatile solid compd., preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aq. medium and administered parenterally, or processed using std. techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A soln. of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the org. soln. (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.

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AN
     2002:676014 CAPLUS
DN
     137:216939
ΤI
     Process of preparing paroxetine and intermediates for use
     therein
IN
     Callewaert, George Leo
PA
     Spurcourt Limited, UK
SO
    PCT Int. Appl., 67 pp.
     CODEN: PIXXD2
DT
    Patent
LΑ
    English
FAN.CNT 1
    PATENT NO. KIND DATE
                                         APPLICATION NO. DATE
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                                         ______
    WO 2002068416 A2
WO 2002068416 A3
PΙ
                           20020906
                                        WO 2002-GB771
                                                         20020222
                           20021121
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
            TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI GB 2001-4583
                    Α
                           20010224
     GB 2001-25119
                      Α
                           20011018
os
    MARPAT 137:216939
GI
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ANSWER 9 OF 21 CAPLUS COPYRIGHT 2003 ACS

L2

- AB A process of prepg. paroxetine, a process for prepg.
 intermediates for use in the prepn. of paroxetine and specific
 intermediates useful in paroxetine prepn. The specific
 intermediates that can be employed include compds. of formulas (I), (II)
 or (III).
- L2 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2003 ACS
- AN 2002:659492 CAPLUS
- DN 137:227829
- TI A general screening method for acidic, neutral, and basic drugs in whole blood using the Oasis MCX column
- AU Yawney, J.; Treacy, S.; Hindmarsh, K. W.; Burczynski, F. J.
- CS Faculty of Pharmacy, University of Manitoba, Winnipeg, MB, R3T 2N2, Can.
- SO Journal of Analytical Toxicology (2002), 26(6), 325-332 CODEN: JATOD3; ISSN: 0146-4760
- PB Preston Publications
- DT Journal
- LA English
- AB Solid-phase extn. (SPE) is becoming a commonly used extn. technique. existing SPE methods ext. a single drug from a relatively clean biol. matrix (e.g., plasma, serum, or urine) using a silica-based column. These methods, however, are generally not satisfactory for forensic applications because the majority of biol. samples are not as clean (e.g., whole blood, bile, tissues). Silica-based columns also may have reproducibility and stability problems. Polymer-based columns have been developed to overcome some of these limitations. In this study, sequential extn. of acidic, neutral, and basic drugs from whole blood using a polymer-based column, Oasis MCX, was undertaken. The extn. procedure developed involved a conditioning step using methanol followed by water; a three-step wash sequence using water, 0.1 M hydrochloric acid, then water/methanol (95:5); and two elution steps. One elution step was for acidic and neutral drugs utilizing acetone/chloroform (1:1), and a second used Et acetate/ ammonium hydroxide (98:2) for basic drugs. Of the drugs tested, 75% were extractable from whole blood and detectable at therapeutic concns. Good recoveries and clean exts. were achieved for the basic drugs; however, the exts. were not as clean for acidic drugs. Unfortunately, the Oasis MCX procedure was not suitable for extg. all drugs (e.g., benzodiazepines). (c) 2002 Preston Publications.
- RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L2 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2003 ACS
- AN 2002:56436 CAPLUS
- DN 136:272591
- TI Simultaneous determination of citalopram, fluoxetine, paroxetine and their metabolites in plasma by temperature-programmed packed capillary liquid chromatography with on-column focusing of large injection volumes
- AU Molander, P.; Thomassen, A.; Kristoffersen, L.; Greibrokk, T.; Lundanes,

Ε.

CS National Institute of Occupational Health, Oslo, N-0033, Norway

SO Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2002), 766(1), 77-87
CODEN: JCBAAI; ISSN: 1570-0232

PB Elsevier Science B.V.

DT Journal

LA English

- A miniaturized temp.-programmed packed capillary liq. chromatog. method AB with on-column large vol. injection and UV detection for the simultaneous detn. of the three selective serotonin reuptake inhibitors citalopram, fluoxetine, paroxetine and their metabolites in plasma is presented. An established reversed-phase C8 solid-phase extn. method was employed, and the sepn. was carried out on a 3.5-.mu.m Kromasil C18 0.32.times.300 mm column with temp.-programming from 35 (3 min) to 100.degree. (10 min) at 1.3.degree./min. The mobile phase consisted of MeCN-45 mM ammonium formate (pH 4.00) (25:75, vol./vol.). The noneluting sample focusing solvent compn. MeCN-45 mM ammonium formate (pH 4.00) (3:97, vol./vol.) allowed injection of 10 .mu.L or more of the plasma exts. The method was validated for the concn. range 0.05-5.0 .mu.M, and the calibration curves were linear with coeffs. of correlation >0.993. The limits of quantification for the antidepressants and their metabolites ranged from 0.05 to 0.26 .mu.M. The within and between assay precision of relative peak height were in the range 2-22 and 2-15% relative std. deviation, resp. The within and between assay recoveries were in the 61-99 and 54-92% range for the antidepressants, resp., and between 52-102 and 51-102% for the metabolites.
- RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L2 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2003 ACS

AN 2001:483439 CAPLUS

DN 135:326896

- TI Methodology for the development of a drug library based upon collision-induced fragmentation for the identification of toxicologically relevant drugs in plasma samples
- AU Lips, A. G. A. M.; Lameijer, W.; Fokkens, R. H.; Nibbering, N. M. M.

CS Agilent Technologies, Amsterdam, 1180 AK, Neth.

SO Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 759(2), 191-207
CODEN: JCBBEP; ISSN: 0378-4347

PB Elsevier Science B.V.

DT Journal

LA English

AB The possibility of creating a robust mass spectral library with use of high-performance lig. chromatog.-atm. pressure-electrospray ionization (HPLC-AP-ESI) for the identification of drugs misused in cases of clin. toxicol. has been examd. Factors reported as influencing the fragmentation induced by "source transport region collision induced dissocn." (CID) have been tested in this study (i.e. solvent, pH, different acids or buffer salts and their concn., different org. modifiers and the modifier concn.). The tests performed on a few "model drugs" were analyzed with use of two different single quadrupole instruments. The large no. of mass spectra obtained appears to be affected by the mobile phase conditions to only a minor extent. This also holds for the mass spectra obtained at two different instruments (labs.). Subsequently breakdown curves have been measured for about 20 randomly chosen drugs by variation of the kinetic energy of their ions in the CID zone through changing the fragmenter voltage. These breakdown curves were used to optimize the fragmenter voltage for each drug. The optimized fragmenter voltages were then applied by use of a variably ramped fragmenter voltage to acquire mass spectra for the library. The chromatog. sepns. were run on a Zorbax Stable bond column using a 10-mM ammonium

formate-acetonitrile gradient method. Spiked blank serum and patient samples with a total of 40 different drugs were extd. with use of a std. basic liq.-liq. extn. (LLE) method. A search of significant peaks in the chromatogram by application of the developed mass spectral library is shown to result in a more than 95% pos. identification.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 13 OF 21 CAPLUS COPYRIGHT 2003 ACS
L2
     2001:300514 CAPLUS
AN
DN
     134:331617
ΤI
     Oil-in-water emulsion compositions for polyfunctional active ingredients
IN
     Chen, Feng-jing; Patel, Mahesh V.
PA
     Lipocine, Inc., USA
SO
     PCT Int. Appl., 82 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
FAN.CNT 1
                 KIND DATE
     PATENT NO.
                                         APPLICATION NO. DATE
     WO 2001028555 A1 20010426
                                         WO 2000-US28835 20001018
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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            LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                           20020808
                                          US 1999-420159
     US 2002107265
                      A1
PRAI US 1999-420159
                      Α
                            19991018
     Pharmaceutical oil-in-water emulsions for delivery of polyfunctional
     active ingredients with improved loading capacity, enhanced stability, and
     reduced irritation and local toxicity are described. Emulsions include an
     aq. phase, an oil phase comprising a structured triglyceride, and an
     emulsifier. The structured triglyceride of the oil phase is substantially
     free of triglycerides having three medium chain (C6-C12) fatty acid
     moieties, or a combination of a long chain triglyceride and a
     polarity-enhancing polarity modifier. The present invention also provides
     methods of treating an animal with a polyfunctional active ingredient,
     using dosage forms of the pharmaceutical emulsions. For example, an
     emulsion was prepd., with cyclosporin A as the polyfunctional active
     ingredient dissolved in an oil phase including a structured triglyceride
     (Captex 810D) and a long chain triglyceride (safflower oil). The compn.
     contained (by wt.) cyclosporin A 1.0, Captex 810D 5.0, safflower oil 5.0,
     BHT 0.02, egg phospholipid 2.4, dimyristoylphosphatidyl glycerol 0.2,
     glycerol 2.25, EDTA 0.01, and water up to 100%, resp.
             THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 6
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 14 OF 21 CAPLUS COPYRIGHT 2003 ACS
L2
ΑN
     2001:136991 CAPLUS
DN
     134:198075
     Triglyceride-free compositions and methods for enhanced absorption of
ΤI
     hydrophilic therapeutic agents
     Patel, Mahesh V.; Chen, Feng-Jing
IN
PA
     Lipocine, Inc., USA
SO
     PCT Int. Appl., 113 pp.
     CODEN: PIXXD2
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DT

LΑ

Patent

English

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KIND DATE
                                             APPLICATION NO. DATE
     PATENT NO.
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     WO 2001012155
                       A1
                              20010222
                                             WO 2000-US18807 20000710
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              LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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     US 6309663
                        В1
                              20011030
                                            US 1999-375636 19990817
     EP 1210063
                        A1
                              20020605
                                              EP 2000-947184 20000710
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              IE, SI, LT, LV, FI, RO, MK, CY, AL
     JP 2003506476
                       T2 20030218
                                             JP 2001-516502
                                                                 20000710
     US 2001024658
                        A1
                              20010927
                                              US 2000-751968 20001229
     US 6458383
                        B2
                              20021001
PRAI US 1999-375636
                       Α
                              19990817
     WO 2000-US18807 W
                              20000710
AB
     The present invention relates to triglyceride-free pharmaceutical compns.,
     pharmaceutical systems, and methods for enhanced absorption of hydrophilic
     therapeutic agents. The compns. and systems include an absorption
     enhancing carrier, where the carrier is formed from a combination of at
     least two surfactants, at least one of which is hydrophilic. A
     hydrophilic therapeutic agent can be incorporated into the compn., or can
     be co-administered with the compn. as part of a pharmaceutical system.
     The invention also provides methods of treatment with hydrophilic
     therapeutic agents using these compns. and systems. For example, when a compn. contg. Cremophor RH40 0.30, Arlacel 186 0.20, Na taurocholate 0.18,
     and propylene glycol 0.32 g, resp., was used, the relative absorption of
     PEG 4000 as a model macromol. drug was enhanced by 991%.
RE.CNT 1
               THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
L2
     ANSWER 15 OF 21 CAPLUS COPYRIGHT 2003 ACS
     2001:12137 CAPLUS
ΑN
DN
     134:61565
TI
     Solid and semi-solid formulations of paroxetine with increased
     stability and bioavailability
IN
     Rosenberg, Joerg; Breitenbach, Joerg; Liepold, Bernd
PA
     Knoll A.-G., Germany
SO
     Ger. Offen., 4 pp.
     CODEN: GWXXBX
DT
     Patent
LΑ
     German
FAN.CNT 1
     PATENT NO.
                      KIND DATE
                                             APPLICATION NO. DATE
                      ----
                                              -----
PI
     DE 19930454
                        A1
                              20010104
                                              DE 1999-19930454 19990702
     WO 2001001956
                        A2
                              20010111
                                              WO 2000-EP5848
                                                                 20000623
                       A3
     WO 2001001956
                              20010712
         W: AU, BR, CA, CN, JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE
     EP 1189614
                              20020327
                                             EP 2000-942125
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, FI
PRAI DE 1999-19930454 A
                              19990702
     WO 2000-EP5848
                        W
                              20000623
AΒ
     The invention concerns solid and semi-solid formulations of
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FAN.CNT 8

paroxetine and its physiol. acceptable salts that contain the mol.-dispersed active substance in a matrix composed of a synthetic polymer with glass transition temp. > 90.degree.C. The invention also concerns the prepn. of the formulations. 80% Of the active substance is bioavailable within 30 min after dosage. Paroxetine or its salt is mixed and melted with the matrix material in the extruder, followed by the forming procedure. In another version paroxetine, ammonium chloride and matrix material are coextruded. The product is used for the prepn. of tablets. Thus 30 wt./wt.% paroxetine hydrochloride and 70 wt./wt.% copovidon (N-vinylpyrrolidone-vinylacetate copolymer 60/40) were processed in a twin-screw extruder at 145.degree.C. The product was used as for the formulation of tablets with the following compn. in wt./wt.%: paroxetine hydrochloride extrudate 38; microcryst. cellulose 15; calciumhydrogen phosphate 35; sodium-croscarmellose 10; highly disperse silica 1; magnesium stearate 1.

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L2
     ANSWER 16 OF 21 CAPLUS COPYRIGHT 2003 ACS
AN
     2000:861473 CAPLUS
DN
     134:32972
     Porous drug matrixes containing polymers and sugars and methods of their
ΤI
     manufacture
     Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak,
IN
     Sarwat; Randall, Greg
PA
     Acusphere, Inc., USA
     PCT Int. Appl., 45 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 2
     PATENT NO.
                     KIND
                           DATE
                                          APPLICATION NO.
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                           -----
                                          -----
     WO 2000072827
                      A2
                           20001207
                                          WO 2000-US14578 20000525
     WO 2000072827
                      A3
                           20010125
         W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
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             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
            MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
            SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
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BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 6395300 B1 20020528 US 1999-433486 19991104 EP 1180020 A2 20020220 EP 2000-939365 20000525 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO BR 2000010984 20020430 BR 2000-10984 20000525 Α 20030107 JP 2003500438 T2 JP 2000-620939 20000525 US 2002041896 A1 20020411 US 2001-798824 20010302 NO 2001005753 20020128 NO 2001-5753 20011126 Α PRAI US 1999-136323P Ρ 19990527 US 1999-158659P Ρ 19991008 US 1999-433486 Α 19991104 US 2000-186310P Ρ 20000302 WO 2000-US14578 W 20000525

AB Drugs, esp. low aq. soly. drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aq. media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aq. soly., in a volatile solvent to form a drug soln., (ii) combining at least one pore forming agent with the drug soln. to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second soln. to yield the porous

matrix of drug. The pore forming agent can be either a volatile liq. that is immiscible with the drug solvent or a volatile solid compd., preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aq. medium and administered parenterally, or processed using std. techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded org. soln. was prepd. by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aq. soln. was prepd. by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The ag. and org. solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prepd. in 5% dextrose soln. at a concn. of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

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L2
    ANSWER 17 OF 21 CAPLUS COPYRIGHT 2003 ACS
    2000:725450 CAPLUS
AN
    133:276365
DN
ΤI
     Ziprasidone metabolite compositions for the treatment of neuroleptic and
     related disorders
     Barberich, Timothy J.; Rubin, Paul D.; Yelle, William E.
IN
PA
     Sepracor Inc., USA
SO
     PCT Int. Appl., 27 pp.
     CODEN: PIXXD2
DT
     Patent
LA
    English
FAN.CNT 1
                                  APPLICATION NO. DATE
     PATENT NO.
                 KIND DATE
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                                          -----
                   A2
A3
PΙ
    WO 2000059489
                           20001012
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            ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
            LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
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                                        EP 2000-920028
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                          20020102
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                                          JP 2000-609053
     JP 2002541098
                     T2
                           20021203
                                                          20000331
PRAI US 1999-127939P
                      P
                           19990406
    WO 2000-US8707
                      W
                           20000331
AB
     The invention relates to novel methods using, and pharmaceutical compns.
     comprising ziprasidone metabolites. The methods and compns. of the
     invention are suitable for the treatment of neuroleptic and related
     disorders. Ziprasidone sulfoxide and ziprasidone sulfone are prepd.,
     their 5-HT2 and dopamine D2 receptor activity studied, and dosage forms
     contg. the compds. are presented.
    ANSWER 18 OF 21 CAPLUS COPYRIGHT 2003 ACS
L2
AN
    2000:457064 CAPLUS
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Salification process for the preparation of an acetate salt of

DN

ΤI

133:73944

paroxetine or paroxetine analogs

```
Craig, Andrew Simon; Jones, David Alan; Man, John
IN
     Smithkline Beecham PLC, UK
PA
     PCT Int. Appl., 15 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
FAN.CNT 1
     PATENT NO.
                     KIND DATE
                                           APPLICATION NO. DATE
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                                        WO 1999-GB4370
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PI
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             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM
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            DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
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     EP 1140912
                      A1
                           20011010
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                            20021008
                                           JP 2000-591034
     JP 2002533459
                      T2
                                                            19991222
PRAI GB 1998-28781
                      Α
                            19981229
                            19991222
     WO 1999-GB4370
                      W
     CASREACT 133:73944; MARPAT 133:73944
OS
GI
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FAN.CNT 1

Ι

Acetate salts of paroxetine and its analogs (I; R1 = substituted ABPh, preferably 3,4-methylenedioxyphenyl) (e.g., paroxetine acetate), useful as therapeutic agents (no data), are prepd. by contacting a soln. of the I (e.g., paroxetine) base with an amine-acetic acid salt (e.g., ammonium acetate). L2ANSWER 19 OF 21 CAPLUS COPYRIGHT 2003 ACS AN 2000:384183 CAPLUS 133:22401 DN ΤI Method of producing paroxetine hydrochloride Craig, Andrew Simon; Jones, David Alan IN PA Smithkline Beecham Plc, UK SO PCT Int. Appl., 18 pp. CODEN: PIXXD2 DT Patent LΑ English

PATENT NO. KIND DATE

APPLICATION NO. DATE

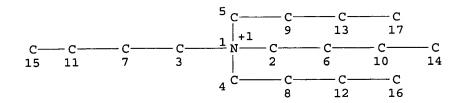
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WO 1999-GB3992 19991130
                       A1
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     WO 2000032593
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                        A1
                             20010926
                                            EP 1999-973026 19991130
     EP 1135382
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     JP 2002531451
                       T2
                              20020924
                                              JP 2000-585235
                                                                 19991130
PRAI GB 1998-26180
                        Α
                              19981130
     WO 1999-GB3992
                        W
                              19991130
AΒ
     The present invention relates to a new process for prepg. pharmaceutically
     active compds. and intermediates therefor. The (-)-trans isomer of
     4-(4'-fluorophenyl)-3-(3",4"-methylenedioxyphenoxymethyl)piperidine (
     paroxetine) is an important compd. having antidepressant and
     anti-Parkinson properties. This compd. is used in therapy as the
     hydrochloride salt to treat inter alia depression, obsessive compulsive
     disorder (OCD) and panic. There is described herein an improved process
     for its prepn. which avoids the generation of impurities caused by the use
     of strong mineral acid to form the salt. A soln. of 5 g
     paroxetine base in in 50 mL propan-2-ol was treated with one
     equiv. of pyridine hydrochloride at room temp. under argon. The resulting
     soln. was stirred rapidly at room temp. whereupon crystn. occur. After 20 min stirring was stopped, and the suspension dild. with propan-2-ol and
     filtered. The solid product was dried in vacuum to give
     paroxetine hydrochloride propan-2-ol solvate (4.83 g).
               THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
L2
     ANSWER 20 OF 21 CAPLUS COPYRIGHT 2003 ACS
AN
     2000:384182 CAPLUS
DN
     133:22400
ΤI
     Process for the preparation of crystalline paroxetine
     hydrochloride propanol solvate
IN
     Craig, Andrew Simon; Jones, Alan David
PA
     Smithkline Beecham PLC, UK
SO
     PCT Int. Appl., 17 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
FAN.CNT 1
     PATENT NO.
                       KIND DATE
                                              APPLICATION NO. DATE
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     WO 2000032592
                              20000608
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                       A1
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              IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
              MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
              SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
              AZ, BY, KG, KZ, MD, RU, TJ, TM
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              CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1133492
                        A1 20010919
                                            EP 1999-973025
                                                                19991126
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO
     JP 2002531450
                        T2
                             20020924
                                              JP 2000-585234
                                                                 19991126
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PRAI GB 1998-26176
                      Α
                           19981128
    WO 1999-GB3968 W
                           19991126
    Cryst. paroxetine hydrochloride (I) propan-2-ol (II) solvate
AB
    having a modified habit that is more easily desolvated to form the
    anhydrate is obtained by crystg. from a soln. of I in II to which has been
    added a habit modifier compd. Form A anhydrate is obtained by heating the
    cryst. solvate of modified habit in a vacuum oven. Suitable habit
    modifiers are carboxylic acids and amine salts. A soln. of I in 170 mL II
    was heated at reflux for 1 h, then cooled to 60.degree. and treated with
    25 mL acetic acid. The reaction mixt. was slowly cooled to room temp.
    with stirring. The resulting white cryst. solid was filtered, washed with
    I and dried under vacuum at 60.degree. for 20 h to give II as acicular
    crystals, contg. 2.8% II.
             THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
    ANSWER 21 OF 21 CAPLUS COPYRIGHT 2003 ACS
L2
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ALL CITATIONS AVAILABLE IN THE RE FORMAT AN 1998:55546 CAPLUS DN 128:119675 Useful formulations of acid addition salt drugs ΤI IN Pero, Ronald W. PA Oxigene, Inc., USA PCT Int. Appl., 81 pp. SO CODEN: PIXXD2 DTPatent LΑ English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE -----____ ----------WO 1997-US10829 19970623 WO 9800159 ΡI A1 19980108 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CA 2258965 AA19980108 CA 1997-2258965 19970623 AU 9734075 A1 19980121 AU 1997-34075 19970623 AU 738165 B2 20010913 EP 954327 **A1** 19991110 EP 1997-930184 19970623 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO JP 2000516204 T2 20001205 JP 1998-504223 19970623 ZA 9705755 Α 19980223 ZA 1997-5755 19970627 PRAI US 1996-673341 19960628 Α WO 1997-US10829 W 19970623 OS MARPAT 128:119675

Disclosed are methods and formulations for administering acid addn. salts of compds. of R1(CH2)nN+HR2R3.cntdot.X- or R1(CH2)nN+R2R3R4.cntdot.X-, wherein R1 comprises an aryl or alkyl group with a hydrogen bond acceptor site accessible to interaction with the tertiary nitrogen or the quaternary ammonium ion, R2, R3 and R4 are alkyl or aryl groups, and X is an anion. A sterile injectable formulation of a liq. vehicle contg. the acid addn. salt in soln. is adjusted in pH for reducing the development of undesirable side effects of the compd. or provided at a pH 5.5-7.0. An i.m. injection contg. the salt at .gtoreq.50 mg/mL and at a pH 5.5-7.0, is safely administered. UV spectral anal. of metoclopramide (I) solns. adjusted in pH 4.8-6.0 showed a very sharp change in maximal absorption of I solns. around pH 5, indicating shifting of equil. between the 2 conformational forms of I, namely, one with the pH sensitive hydrogen bond present and one without it.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT



ENTER (DIS), GRA, NOD, BON OR ?:end L1 STRUCTURE CREATED

=> s 11

SAMPLE SEARCH INITIATED 12:10:23 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2314 TO ITERATE

43.2% PROCESSED 1000 ITERATIONS INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS:

43396 TO 49164

PROJECTED ANSWERS:

12478 TO 15660

L2 50 SEA SSS SAM L1

=> s l1 ful

FULL SEARCH INITIATED 12:10:28 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 46178 TO ITERATE

100.0% PROCESSED 46178 ITERATIONS

14667 ANSWERS

50 ANSWERS

SEARCH TIME: 00.00.01

L3 14667 SEA SSS FUL L1

=> s 13 and benzodioxo?

119638 BENZODIOXO?

L4 22 L3 AND BENZODIOXO?

=> d 1-22

L4 ANSWER 1 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 446301-42-4 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, salt with 1,3-benzodioxol-5-ol (1:1) (9CI) (CA INDEX NAME)

MF C16 H36 N . C7 H5 O3

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 136135-09-6 CMF C7 H5 O3

CM 2

CRN 10549-76-5 CMF C16 H36 N

n-Bu | n-Bu-N+Bu-n | n-Bu

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L4 ANSWER 2 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 263719-45-5 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, salt with 5-nitro-1,3-benzenedicarboxylic acid, compd. with stereoisomer of 3,3',3'',3'''[5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(4,7,10,13-tetraoxatetradec-1-yl)-2,24:3,23-dimetheno-1H,25H,27H,29H-bis[1,4]dioxonino[6,5-j:6',5'-j']benzo[1,2-e:5,4-e']bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis[benzenecarboximidamide] tetrahydrochloride (4:2:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,3-Benzenedicarboxylic acid, 5-nitro-, ion(2-), bis(N,N,N-tributyl-1-butanaminium), compd. with stereoisomer of 3,3',3'',3'''[5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(4,7,10,13-tetraoxatetradec-1-yl)-2,24:3,23-dimetheno-1H,25H,27H,29H-bis[1,4]dioxonino[6,5-j:6',5'-j']benzo[1,2-e:5,4-e']bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis[benzenecarboximidamide] tetrahydrochloride (2:1) (9CI)

CN Benzenecarboximidamide, 3,3',3'',3'''-[5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(4,7,10,13-tetraoxatetradec-1-yl)-2,24:3,23-dimetheno-1H,25H,27H,29H-bis[1,4]dioxonino[6,5-j:6',5'-j']benzo[1,2-e:5,4-e']bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis-, tetrahydrochloride, stereoisomer, compd. with N,N,N-tributyl-1-butanaminium salt with 5-nitro-1,3-benzenedicarboxylic acid (1:4:2) (9CI)

MF C104 H136 N8 O24 . 2 C16 H36 N . C8 H3 N O6 . 4 Cl H

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 263718-39-4 (263719-50-2) CMF C104 H136 N8 O24 . 4 Cl H

PAGE 1-B

PAGE 2-B

∠OMe

OMe

●4 HCl

CM 2

CRN 263159-72-4

CMF C16 H36 N . 1/2 C8 H3 N O6

CM 3.

CRN 263159-71-3 CMF C8 H3 N O6

CM 4

CRN 10549-76-5 CMF C16 H36 N

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L4 ANSWER 3 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 263719-44-4 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, salt with 5-nitro-1,3-benzenedicarboxylic acid, compd. with stereoisomer of 3,3',3'',3'''[5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(4,7,10,13-tetraoxatetradec-1-yl)-2,24:3,23-dimetheno-1H,25H,27H,29H-bis[1,4]dioxonino[6,5-j:6',5'-j']benzo[1,2-e:5,4-e']bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis[benzenecarboximidamide] tetrahydrochloride (2:1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,3-Benzenedicarboxylic acid, 5-nitro-, ion(2-), bis(N,N,N-tributyl-1-butanaminium), compd. with stereoisomer of 3,3',3'',3'''[5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(4,7,10,13-tetraoxatetradec-1-yl)-2,24:3,23-dimetheno-1H,25H,27H,29H-bis[1,4]dioxonino[6,5-j:6',5'-j']benzo[1,2-e:5,4-e']bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis[benzenecarboximidamide] tetrahydrochloride (1:1) (9CI)

CN Benzenecarboximidamide, 3,3',3'',3'''-[5,6,10,11,15,16,20,21-octahydro-1,25,27,29-tetrakis(4,7,10,13-tetraoxatetradec-1-yl)-2,24:3,23-dimetheno-1H,25H,27H,29H-bis[1,4]dioxonino[6,5-j:6',5'-j']benzo[1,2-e:5,4-e']bis[1,4]benzodioxonin-8,13,18,32-tetrayl]tetrakis-, tetrahydrochloride, stereoisomer, compd. with N,N,N-tributyl-1-butanaminium salt with 5-nitro-1,3-benzenedicarboxylic acid (1:2:1) (9CI)

MF C104 H136 N8 O24 . C16 H36 N . 1/2 C8 H3 N O6 . 4 Cl H

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 263718-39-4 (263719-50-2) CMF C104 H136 N8 O24 . 4 Cl H

PAGE 1-B

PAGE 2-B

_ OMe

OMe

●4 HCl

CM 2

CRN 263159-72-4

CMF C16 H36 N . 1/2 C8 H3 N O6

CM 3

CRN 263159-71-3 CMF C8 H3 N O6

CM 4

CRN 10549-76-5 CMF C16 H36 N

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L4 ANSWER 4 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 254905-00-5 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, 1-(1,3-benzodioxole-5-methanamine-.kappa.N5)-2,3,4,5,6,7,8,9,10,11,12-undecahydrododecaborate(1-) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Dodecaborate(1-), 1-(1,3-benzodioxole-5-methanamine-.kappa.N5)2,3,4,5,6,7,8,9,10,11,12-undecahydro-, N,N,N-tributyl-1-butanaminium
(9CI)

MF C16 H36 N . C8 H20 B12 N O2

SR CA

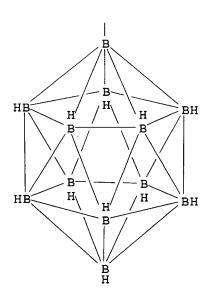
LC STN Files: CA, CAPLUS

CM 1

CRN 254904-99-9

CMF C8 H20 B12 N O2

CCI RIS



PAGE 2-A

CM 2

CRN 10549-76-5 CMF C16 H36 N

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L4 ANSWER 5 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 254904-90-0 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, 1-[(.alpha.E)-1,3-benzodioxole-5-methanimine-.kappa.N5]-2,3,4,5,6,7,8,9,10,11,12-undecahydrododecaborate(1-) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Dodecaborate(1-), 1-[(.alpha.E)-1,3-benzodioxole-5-methanimine-.kappa.N5]-2,3,4,5,6,7,8,9,10,11,12-undecahydro-, N,N,N-tributyl-1-butanaminium (9CI)

MF C16 H36 N . C8 H18 B12 N O2

SR CA

LC STN Files: CA, CAPLUS

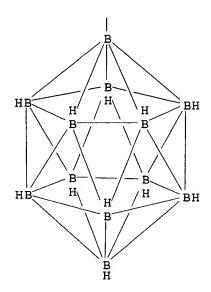
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CRN 254904-89-7

CMF C8 H18 B12 N O2

CCI RIS

PAGE 1-A



CM 2

CRN 10549-76-5 CMF C16 H36 N

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L4 ANSWER 6 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 213322-12-4 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, salt with stereoisomer of 1,21,23,25-tetramethyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrol, compd. with pyrazine and stereoisomer of 1,21,23,25-tetramethyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrol (4:1:1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

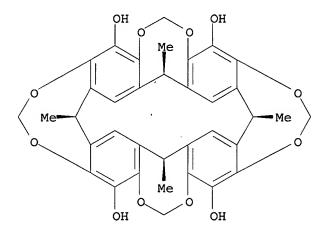
CN 2,20:3,19-Dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-

CN 2,20:3,19-Dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrol,
1,21,23,25-tetramethyl-, ion(4-), stereoisomer, tetrakis(N,N,N-tributyl-1butanaminium), compd. with pyrazine and stereoisomer of
1,21,23,25-tetramethyl-2,20:3,19-dimetheno-1H,21H,23H,25Hbis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin7,11,15,28-tetrol (1:1:1) (9CI)

CN 2,20:3,19-Dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrol, 1,21,23,25-tetramethyl-, stereoisomer, compd. with pyrazine and N,N,N-tributyl-1-butanaminium salt with stereoisomer of 1,21,23,25-tetramethyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrol (1:1:4:1) (9CI)

CNPyrazine, compd. with stereoisomer of 1,21,23,25-tetramethyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrol and N,N,N-tributyl-1-butanaminium salt with stereoisomer of 1,21,23,25-tetramethyl-2,20:3,19-dimetheno-1H,21H,23H,25Hbis [1,3] dioxocino [5,4-i:5',4'-i'] benzo [1,2-d:5,4-d'] bis [1,3] benzodioxocin-7,11,15,28-tetrol (1:1:4:1) (9CI) FS STEREOSEARCH C36 H32 O12 . C36 H28 O12 . 4 C16 H36 N . C4 H4 N2 MF SR LCSTN Files: CA, CAPLUS CM 1 CRN 161616-54-2 CMF C36 H32 O12

Relative stereochemistry.



CRN 290-37-9 CMF C4 H4 N2



CM 3

CRN 213322-11-3

CMF C36 H28 O12 . 4 C16 H36 N

CM 4

CRN 213322-10-2

CMF C36 H28 O12

Relative stereochemistry.

CM 5

CRN 10549-76-5 CMF C16 H36 N

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L4 ANSWER 7 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 213322-11-3 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, salt with stereoisomer of 1,21,23,25-tetramethyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrol (4:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2,20:3,19-Dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrol,
1,21,23,25-tetramethyl-, ion(4-), stereoisomer, tetrakis(N,N,N-tributyl-1-butanaminium) (9CI)

FS STEREOSEARCH

MF C36 H28 O12 . 4 C16 H36 N

CI COM

SR CA

CM 1

CRN 213322-10-2 CMF C36 H28 O12

Relative stereochemistry.

CM 2

CRN 10549-76-5 CMF C16 H36 N

L4 ANSWER 8 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 210779-70-7 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, iodide, compd. with stereoisomer of N,N'',N'''',N''''-[(1,21,23,25-tetrapentyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrayl)tetrakis(methylene)]tetrakis[N'-[8-(2-nitrophenoxy)octyl]urea] (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Urea, N,N''',N''''', N''''''-[(1,21,23,25-tetrapentyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrayl)tetrakis(methylene)]tetrakis[N'-[8-(2-nitrophenoxy)octyl]-, stereoisomer, compd. with N,N,N-tributyl-1-butanaminium iodide (1:1) (9CI)

MF C116 H156 N12 O24 . C16 H36 N . I

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 210685-21-5 CMF C116 H156 N12 O24

PAGE 1-B

PAGE 2-B

NO2

CM 2

CRN 311-28-4 (10549-76-5) CMF C16 H36 N . I

• I-

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L4 ANSWER 9 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 210779-69-4 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, bromide, compd. with stereoisomer of N,N'',N''''-[(1,21,23,25-tetrapentyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrayl)tetrakis(methylene)]tetrakis[N'-[8-(2-nitrophenoxy)octyl]urea] (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Urea, N,N'',N'''',N'''''-[(1,21,23,25-tetrapentyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrayl)tetrakis(methylene)]tetrakis[N'-[8-(2-nitrophenoxy)octyl]-, stereoisomer, compd. with N,N,N-tributyl-1-butanaminium bromide (1:1) (9CI)

MF C116 H156 N12 O24 . C16 H36 N . Br

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 210685-21-5 CMF C116 H156 N12 O24

PAGE 1-B

PAGE 2-B

CM 2

CRN 1643-19-2 (10549-76-5) CMF C16 H36 N . Br

• Br-

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L4 ANSWER 10 OF 22 REGISTRY COPYRIGHT 2003 ACS

RN 210779-68-3 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, chloride, compd. with stereoisomer of N,N'',N'''',N''''-[(1,21,23,25-tetrapentyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrayl)tetrakis(methylene)]tetrakis[N'-[8-(2-nitrophenoxy)octyl]urea] (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Urea, N,N'',N'''',N'''''-[(1,21,23,25-tetrapentyl-2,20:3,19-dimetheno-1H,21H,23H,25H-bis[1,3]dioxocino[5,4-i:5',4'-i']benzo[1,2-d:5,4-d']bis[1,3]benzodioxocin-7,11,15,28-tetrayl)tetrakis(methylene)]tetrakis[N'-[8-(2-nitrophenoxy)octyl]-, stereoisomer, compd. with N,N,N-tributyl-1-butanaminium chloride (1:1) (9CI)

MF C116 H156 N12 O24 . C16 H36 N . Cl

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 210685-21-5 CMF C116 H156 N12 O24

PAGE 1-B

PAGE 2-B

CRN 1112-67-0 (10549-76-5) CMF C16 H36 N . C1

● Cl-

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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137:169504 CASREACT
AN
     Preparation of N-methylparoxetine by the reaction of sesamol-
ΤI
     tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-N-
     methylpiperidine followed by alkaline hydrolysis
     Finkelstein, Nina
IN
     Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,
PA
     Inc.
SO
     PCT Int. Appl., 16 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
IC
     ICM C07D405-12
     ICS C07D211-22
     28-5 (Heterocyclic Compounds (More Than One Hetero Atom))
CC
     Section cross-reference(s): 45
FAN.CNT 1
    PATENT NO.
                                         APPLICATION NO. DATE
                    KIND DATE
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                                          -----
                                         WO 2002-US3223 20020204
     WO 2002062790
                     A1 20020815
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
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         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                         US 2002-67160
     US 2002151567
                      A1
                            20021017
                                                          20020202
PRAI US 2001-266498P
                     20010205
     US 2001-277587P 20010321
os
     MARPAT 137:169504
     N-methylparoxetine is prepd. in high yield and selectivity by the reaction
     of sesamol-tetrabutylammonium salt in toluene and isopropanol with
     4-(4-fluorophenyl)-3-chloromethyl-N-methylpiperidine, followed by alk.
     hydrolysis.
ST
     methylparoxetine prepn
IT
     Hydrolysis
        (base; prepn. of N-methylparoxetine by the reaction of
        sesamol-tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-
        N-methylpiperidine followed by alk. hydrolysis)
IT
     Quaternary ammonium compounds, preparation
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of N-methylparoxetine by the reaction of sesamol-
        tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-N-
        methylpiperidine followed by alk. hydrolysis)
IT
     533-31-3, Sesamol
                        393809-76-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of N-methylparoxetine by the reaction of sesamol-
        tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-N-
        methylpiperidine followed by alk. hydrolysis)
IT
     2052-49-5, Tetrabutylammonium hydroxide
     RL: RCT (Reactant); RGT (Reagent); RACT (Reactant or reagent)
        (prepn. of N-methylparoxetine by the reaction of sesamol-
        tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-N-
        methylpiperidine followed by alk. hydrolysis)
IT
     446301-42-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of N-methylparoxetine by the reaction of sesamol-
```

tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-N-methylpiperidine followed by alk. hydrolysis)

IT 110429-36-2P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-methylparoxetine by the reaction of sesamol-

tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-N-methylpiperidine followed by alk. hydrolysis)

IT 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 75-05-8,

Acetonitrile, uses 108-88-3, Toluene, uses

RL: NUU (Other use, unclassified); USES (Uses)

(solvent; prepn. of N-methylparoxetine by the reaction of

sesamol-tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-N-methylpiperidine followed by alk. hydrolysis)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Agafonova; SU 1816754 CAPLUS Accession No 1995:339464 1993 CAPLUS
- (2) Smithkline Beecham P L C; WO 0206275 A1 2002 CAPLUS

RX(1) OF 1 A + B ===> C

C YIELD 86%

RX(1) RCT A 533-31-3

STAGE (1)

RGT D 2052-49-5 Bu4NOH SOL 67-63-0 Me2CHOH, 67-56-1 MeOH

STAGE (2)

RCT B 393809-76-2 SOL 108-88-3 PhMe STAGE(3) RGT E 1310-73-2 NaOH SOL 7732-18-5 Water PRO C 110429-36-2

```
2002:615607 CAPLUS
AN
     137:169504
DN
     Preparation of N-methylparoxetine by the reaction of sesamol-
TI
     tetrabutylammonium salt with 4-(4-fluorophenyl)-3-chloromethyl-N-
     methylpiperidine followed by alkaline hydrolysis
IN
     Finkelstein, Nina
     Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,
PΑ
     Inc.
SO
     PCT Int. Appl., 16 pp.
     CODEN: PIXXD2
DT
     Patent
    English
LA
FAN.CNT 1
                    KIND DATE
     PATENT NO.
                                         APPLICATION NO. DATE
     -----
                                          -----
     WO 2002062790
                     A1 20020815
                                         WO 2002-US3223 20020204 <--
PI
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
            · TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                           20021017
                                         US 2002-67160 20020202
     US 2002151567
                     A1
PRAI US 2001-266498P
                      Р
                           20010205
     US 2001-277587P
                     P
                           20010321
     CASREACT 137:169504; MARPAT 137:169504
OS
     N-methylparoxetine is prepd. in high yield and selectivity by the reaction
AB
     of sesamol-tetrabutylammonium salt in toluene and isopropanol with
     4-(4-fluorophenyl)-3-chloromethyl-N-methylpiperidine, followed by alk.
     hydrolysis.
RE.CNT 2
             THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> analyze 11
ENTER ANSWER NUMBER OR RANGE (1-):1
ENTER DISPLAY CODE (TI) OR ?:rn
L2
           ANALYZE L1 1 RN :
                                  9 TERMS
=> fil req
COST IN U.S. DOLLARS
                                                SINCE FILE
                                                                TOTAL
                                                     ENTRY
                                                              SESSION
FULL ESTIMATED COST
                                                     14.67
                                                                14.88
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
                                                SINCE FILE
                                                                TOTAL
                                                     ENTRY
                                                             SESSION
CA SUBSCRIBER PRICE
                                                     -0.65
                                                               -0.65
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FILE 'REGISTRY' ENTERED AT 11:55:29 ON 19 JUN 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 JUN 2003 HIGHEST RN 532924-24-6 DICTIONARY FILE UPDATES: 17 JUN 2003 HIGHEST RN 532924-24-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s 12

L3 9 L2

=> d 1-9

L3 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2003 ACS

RN 446301-42-4 REGISTRY

CN 1-Butanaminium, N,N,N-tributyl-, salt with 1,3-benzodioxol-5-ol (1:1) (9CI) (CA INDEX NAME)

MF C16 H36 N . C7 H5 O3

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 136135-09-6 CMF C7 H5 O3

CM 2

CRN 10549-76-5 CMF C16 H36 N

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2003 ACS
- RN 393809-76-2 REGISTRY
- CN Piperidine, 3-(chloromethyl)-4-(4-fluorophenyl)-1-methyl-, (3R,4S)-rel-(9CI) (CA INDEX NAME)
- FS STEREOSEARCH
- MF C13 H17 Cl F N
- CI COM
- SR CA

LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Relative stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 2 REFERENCES IN FILE CA (1957 TO DATE)
- 2 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2003 ACS
- RN 110429-36-2 REGISTRY
- CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-methyl-, (3S,4R)- (9CI) (CA INDEX NAME)

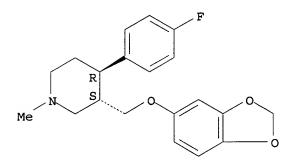
OTHER CA INDEX NAMES:

CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-methyl-, (3S-trans)-

OTHER NAMES:

- CN (-)-trans-4-(4-Fluorophenyl)-3-(3,4-methylenedioxyphenoxymethyl)-1-methylpiperidine
- CN N-Methylparoxetine
- FS STEREOSEARCH
- MF C20 H22 F N O3
- SR CA
- LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMCATS, USPAT7ULL (*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 13 REFERENCES IN FILE CA (1957 TO DATE)
- 13 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2003 ACS
- RN 2052-49-5 REGISTRY
- CN 1-Butanaminium, N,N,N-tributyl-, hydroxide (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Ammonium, tetrabutyl-, hydroxide (8CI)

```
Tetrabutylammonium hydroxide (6CI)
CN
OTHER NAMES:
     Tetra-n-butylammonium hydroxide
CN
     151883-00-0, 107716-44-9
DR
     C16 H36 N . H O
MF
CI
     COM
                 AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS,
LC
     STN Files:
       CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DETHERM*, DIOGENES,
       EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NIOSHTIC, PIRA, PROMT,
       RTECS*, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
CRN
     (10549 - 76 - 5)
   n-Bu
       +
Bu-n
n-Bu-N
   n-Bu
   ● OH -
            1561 REFERENCES IN FILE CA (1957 TO DATE)
              31 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1563 REFERENCES IN FILE CAPLUS (1957 TO DATE)
              30 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
    ANSWER 5 OF 9 REGISTRY COPYRIGHT 2003 ACS
L3
RN
    533-31-3 REGISTRY
CN
    1,3-Benzodioxol-5-ol (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN
    Phenol, 3,4-(methylenedioxy)- (7CI, 8CI)
    Sesamol (6CI)
CN
OTHER NAMES:
CN
     3,4-(Methylenedioxy)phenol
CN
     4-Hydroxy-1,2-methylenedioxybenzene
     5-Hydroxy-1,3-benzodioxole
CN
FS
     3D CONCORD
MF
    C7 H6 O3
CI
     COM
LC
     STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*,
       IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NAPRALERT, NIOSHTIC, PIRA, PROMT,
       RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources: EINECS**, NDSL**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
```

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918 REFERENCES IN FILE CAPLUS (1957 TO DATE)
               28 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
     ANSWER 6 OF 9 REGISTRY COPYRIGHT 2003 ACS
L3
     108-88-3 REGISTRY
RN
     Benzene, methyl- (9CI) (CA INDEX NAME)
CN
OTHER CA INDEX NAMES:
     Toluene (8CI)
CN
OTHER NAMES:
     1-Methylbenzene
CN
CN
     Antisal la
CN
     CP 25
CN
     CP 25 (solvent)
     Methacide
CN
CN
     Methylbenzene
     Methylbenzol
CN
CN
     Phenylmethane
CN
     Toluol
FS
     3D CONCORD
MF
     C7 H8
CI
     COM
                   ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS,
LC
       BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,
       CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB,
       DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2,
       ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA,
       PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT2,
       USPATFULL, VETU, VTB
          (*File contains numerically searchable property data)
                      DSL**, EINECS**, TSCA**
     Other Sources:
          (**Enter CHEMLIST File for up-to-date regulatory information)
```

19 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

917 REFERENCES IN FILE CA (1957 TO DATE)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

71127 REFERENCES IN FILE CA (1957 TO DATE)
676 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
71243 REFERENCES IN FILE CAPLUS (1957 TO DATE)
24 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
ANSWER 7 OF 9 REGISTRY COPYRIGHT 2003 ACS
L3
     75-05-8 REGISTRY
RN
CN
    Acetonitrile (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
    Acetonitrile cluster
CN
CN
    Cyanomethane
CN
    Ethanenitrile
CN
    Ethyl nitrile
CN
    Methane, cyano-
CN
    Methanecarbonitrile
```

```
Methyl cyanide
CN
     Methyl cyanide (MeCN)
CN
     3D CONCORD
FS
     54841-72-4
DR
     C2 H3 N
MF
CI
     COM
                    AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS,
LC
     STN Files:
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT2, ENCOMPPAT2,
       GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO,
       SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT7, USPATFULL, VTB
          (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
          (**Enter CHEMLIST File for up-to-date regulatory information)
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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
            28979 REFERENCES IN FILE CA (1957 TO DATE)
              384 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            29048 REFERENCES IN FILE CAPLUS (1957 TO DATE)
               10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
     ANSWER 8 OF 9 REGISTRY COPYRIGHT 2003 ACS
L3
     67-63-0 REGISTRY
RN
                        (CA INDEX NAME)
CN
     2-Propanol (9CI)
OTHER CA INDEX NAMES:
     Isopropyl alcohol (8CI)
OTHER NAMES:
CN
     1-Methylethanol
CN
     1-Methylethyl alcohol
CN
     2-Hydroxypropane
CN
     2-Propyl alcohol
CN
     Alcojel
CN
     Alcosolve 2
CN
     Autosept
CN
     Avantin
CN
     Avantine
CN
     Combi-Schutz
     Dimethylcarbinol
CN
CN
     Hartosol
CN
     Imsol A
CN
     IPA
CN
     IPS 1
CN
     IPS 1 (alcohol)
CN
     iso-Propanol
CN
     iso-Propyl alcohol
CN
     Isohol
CN
     Isopropanol
CN
     Lutosol
CN
     n-Propan-2-ol
CN
     Petrohol
CN
     PRO
CN
     Propol
CN
     sec-Propanol
CN
     sec-Propyl alcohol
     Sterisol Hand Disinfectant
CN
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CN
     Takineocol
CN
     Tokuso IPA
     Virahol
CN
     3D CONCORD
FS
DR
     8013-70-5
     C3 H8 O
MF
CI
     COM
                   ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS,
LC
     STN Files:
       BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB,
       DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2,
       ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB,
       IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA,
       PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN,
       USPAT2, USPATFULL, VETU, VTB
          (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
          (**Enter CHEMLIST File for up-to-date regulatory information)
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H<sub>3</sub>C-CH-CH<sub>3</sub>
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            42748 REFERENCES IN FILE CA (1957 TO DATE)
              610 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            42837 REFERENCES IN FILE CAPLUS (1957 TO DATE)
                8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
L3
     ANSWER 9 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN
     67-56-1 REGISTRY
CN
     Methanol (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
     Bieleski's solution
CN
CN
     Carbinol
CN
     Methanol cluster
     Methyl alcohol
CN
CN
     Methyl hydroxide
CN
     Methylol
CN
     Monohydroxymethane
CN
     Solutions, Bieleski's
ÇN
     Wood alcohol
FS
     3D CONCORD
DR
     54841-71-3
MF
     C H4 O
CI
LC
                   ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,
       CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB,
       DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2,
       ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB,
       IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA,
       PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2,
       USPATFULL, VETU, VTB
          (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
          (**Enter CHEMLIST File for up-to-date regulatory information)
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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

109627 REFERENCES IN FILE CA (1957 TO DATE)
1350 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
109764 REFERENCES IN FILE CAPLUS (1957 TO DATE)
20 REFERENCES IN FILE CAOLD (PRIOR TO 1967)